

ABSTRACT OF THE INVENTION

The invention provides methods for conducting hybridizations having increased selectivity of hybridization using substrates upon which probe nucleic acids are immobilized. The methods of this invention can be used to increase selectivity in nucleic acid diagnostic devices, such as biosensors and microarrays. The invention provides increased selectivity through control of the substrate surface chemistry and in particular, through control of the density of nucleic acids and other oligomers immobilized on a surface. The invention provides improved signal to noise in hybridization assays *via* enhanced differences in signal magnitude generated for fully matched target nucleic acid compared to partially matched target nucleic acid prior to signal processing. Specifically, invention provides methods for using substrates having medium-high to high immobilization densities to achieve higher hybridization. The methods and substrates of this invention are particularly well-suited to assays for genetic targets in samples that contain genetic species that are very similar in nucleic acid sequence to the genetic target. The methods and substrates of this invention are also well-suited for single nucleotide polymorphism (SNP) analysis.